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10/523,318	02/01/2005	Gerard Brady	2000301.124 US1	7650

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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/523,318	BRADY, GERARD	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-114* is/are pending in the application.

4a) Of the above claim(s) *58-66,69-71 and 98-114* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67,68 and 72-97* is/are rejected.

7)☒ Claim(s) *67* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-57 have been canceled as filed on 2/1/05;

Claims 58-114 are currently pending.

Claims 58-66, 69-71 and 98-114 have been withdrawn.

Claims 67, 68 and 72-97 are being examined in this application.

Election/Restrictions

2. Applicant's election of Group 2 invention (Claims 67, 68, and 72-97) in the reply filed on 4/12/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 58-66, 69-71 and 98-114 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/12/07.

Priority

4. This application is filed under 35 U.S.C 371 of PCT/GB03/02710 (filed on 6/23/2003).

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The IDS filed on 3/21/05 have been considered. See the attached PTO 1449 forms.

Specification

7. The disclosure is objected to because of the following informalities: The section for "Brief Description of Drawings" is omitted from the instant disclosure. See MPEP 608.01(f).

Appropriate correction is required.

8. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. MPEP 608.01

Claim Objections

9. Claim 67 is objected to because the said claim depends on a non-elected claim (Claim 58) that is drawn to a non-elected invention. Appropriate correction is requested.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

11. Claims 67, 68 and 72-97 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite "a method of producing a collection of labeled target DNA molecules according to claim 58, comprising: (i) subjecting double-stranded DNA molecules to exonuclease digestion to produce a collection of essentially single-stranded DNA molecules; and (ii) labeling the single-stranded molecules."

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions, including chemical inventions, and because the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide a description of the compound sufficient to

distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

The instant claims (e.g. Claims 67 and 79) are drawn to a genus of methods of producing labeled single stranded DNA using "exonuclease" from double-stranded DNA. The instant claims are broad and encompassing any "double stranded DNA", and any "exonuclease". Neither the instant specification nor the claims have demonstrated common structure and/or

function for the claimed genuses DNA molecules and exonucleases used for the claimed methods. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genuses.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. (see MPEP 2163 II).

In this case, the instant application only disclosed using the "Exonuclease III" for digesting double stranded nucleic acid. The reaction conditions for other "exonucleases" cannot be predicted from the reaction with "Exonuclease III". Even for Exonuclease III, the exonuclease reaction will only proceed under certain conditions. For example, Tabor (Current Protocols in Molecular Biology. Unit 3.11, p. 3.11.1-3.11.4; 1987), teaches exo III preferentially degrade from duplex DNA having a 3'-recessed end as opposed to one with a 5'-recessed end (p. 3.11.4, para 6). Thus, it is highly unpredictable how "Exonuclease III" degrades double stranded DNA molecules.

Tabor also teaches other "exnucleases", which have different degradation properties and requirements (see the Entire document). The reference teaches some exonucleases would only degrade single stranded DNA (e.g. p. 3.11.1), which cannot be used to degrade double stranded DNA. However, the instant claim language is broad to encompass degradation of any double stranded DNA with any "exonuclease".

In addition, Lehman et al (Journal of Biological Chemistry. Vol. 239: 2628-2636; 1964) also teach that degradation of Exonuclease I requires a free 3'-hydroxyl end (p. 2628, col.1, para 4), and DNA with a phosphryl or acetyl group are resistant to the action of exonuclease I (p. 2636, col.1, para4). Thus, digestion of any double stranded DNA using any exonuclease is highly unpredictable.

The recited method of producing single stranded DNA from double stranded DNA using exonuclease is essentially a trial and error process that would involve identifying appropriate DNA molecules that are compatible with appropriate exonucleases. As discussed above, not all double stranded DNA can be degraded to single stranded DNA using any exonuclease. Therefore, applicants are not in possession of the entire claimed genus of methods of digesting any double stranded DNA with any exonucleases. Applicant's claimed scope represents only an invitation to experiment regarding possible exonucleases that might be used for the purpose of digesting double stranded DNA molecules.

Second paragraph of 35 U.S.C. 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 67, 68 and 72-97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A.) Claim 67 recites the term "essentially", which is indefinite because it is a relative term. The term "essentially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear, for example, to what percentage of the total DNA is to be "single-stranded" as produced by the instant claimed method.

B.) Claim 72 recites the phrase "partial digestion", which is indefinite. The term " partial digestion" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear to which degree the "double-stranded DNA molecules" are digested.

C.) Claim 74 in general is unclear, and thus rendering the claim indefinite. The claim recites "one strand of the double-stranded DNA molecules incorporates a restriction site", which is not clear because restriction site requires sequences from both strands of the DNA molecules. (see description of "Restriction Enzyme" from Wikipedia downloaded from ://en.wikipedia.org/wiki/Restriction_enzyme, on 7/4/07). The claim also recites "the molecules are treated with the appropriate restriction enzyme to produce double-stranded molecules having a sticky end", which recitation is unclear. It seems that the claim is reciting that "a single restriction enzyme" was used to produce sticky ends in the double stranded molecule, howver, the claim also seem to recite that one of the ends is a "blunt end" instead of a "sticky end".

Claim 74 recites the limitation "the blunt end". There is insufficient antecedent basis for this limitation in the claim

Claim 74 recites the limitation "the appropriate restriction enzyme". There is insufficient antecedent basis for this limitation in the claim.

Claim 74 recites the limitation "the molecules" in line 2. There is insufficient antecedent basis for this limitation in the claim. It is not clear to which "molecules" (e.g. double-stranded DNA, or single stranded DNA, etc.) the term is referring.

Claim 74 recites the limitation "the blunt end". There is insufficient antecedent basis for this limitation in the claim.

D.) Claim 75 recites the limitation "the 3'-5' strand". There is insufficient antecedent basis for this limitation in the claim. It is also not clear to which strand in the double-stranded molecule the term is referring.

E.) Claim 79 recites the limitation "the sample". There is insufficient antecedent basis for this limitation in the claim.

F.) Claims 79 and 82 recite the phrase "limiting concentrations", which is indefinite. The term "limiting concentration" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear to what specific concentration is considered "limiting" and encompassed by the instant claims.

G.) Claims 82 and 83 recite the limitation "the poly A tail". There is insufficient antecedent basis for this limitation in the claims.

H.) Claim 68 recite the limitation "the action of terminal transferase". There is insufficient antecedent basis for this limitation in the claims.

I.) Claim 81 recites the phrase "wherein the acetate buffer comprises Tris acetate incorporating potassium acetate...", which is unclear. It is not clear how the potassium acetate or magnesium acetate are "incorporated" in the "tris acetate".

J.) Claims 79-97 recite a method of preparing cDNA from mRNA using various steps and reagents. Each of the method steps and their corresponding reagents (i.e. buffers) are not clearly recited. For example, the first step (i.e. step a) of Claim 79 seems to recite the compleat process of generating cDNA, which would include reactions such as reverse transcription, terminal transferase reaction to add primer tails, and PCR reaction to amplify the cDNA population. Each of the said reactions would require different reaction conditions. However, the instant claim 79 also seems to recite additional steps of "homopolymer tailing" (e.g. addition of primer to DNA fragments), and an amplifications step. The buffer conditions recited in the instant claims (e.g. Claims 89 and 96 reciting conditions for steps b and c) seem to encompass reaction conditions for step a) of Claim 79. Furthermore, claim 97 recites buffer conditions for both terminal transferase reaction (i.e. one of the exemplary reactions for "hompolymer tailing") and DNA amplification reaction (i.e. using DNA polymerase), which seems to be in conflict with the separate steps listed in the instant claim 79. Thus, one of ordinary skill in the art would not be able to determine the required steps for the claimed method.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(Note: the instant claim numbers are in bold font.)

Liao

16. Claims 67 and 72-79 are rejected under 35 U.S.C. **102(b)** as anticipated by or, in the alternative, under 35 U.S.C. **103(a)** as obvious over Liao et al (Biochemistry. Vol. 20: 1646-1652; 1981).

The instant claims recite "a method of producing a collection of labeled target DNA molecules according to claim 58, comprising: (i) subjecting double-stranded DNA molecules to exonuclease digestion to produce a collection of essentially single-stranded DNA molecules; and (ii) labeling the single-stranded molecules."

The instant Claim 58 recites "a collection of labeled target DNA moelcuels with are exonuclease derivative of double-stranded DNA." (Note: Claim 58 has been withdrawn due to non-elected invention, and Claim 58 is not being treated on the merits of the said claims in the instant office action.) Because Claim 58 recite the end product of the instant claimed method (as

recited in Claim 67, the instant claim 58 does not offer any additional structurally limitation to the recited in method of the instant claim 67.

Liao et al, throughout the publication, teach a method of producing single stranded and labeled DNA from double stranded DNA molecules using exonuclease digestion (Abstract). The reference teaches generation of "double-stranded complementary deoxyribonucleic acid (cDNA)" (Abstract), and cloned into a plasmid (e.g. Abstract; p. 1647, col.1; Figure 5). The reference teaches the double stranded cDNA were subjected to digestion by "exonuclease III" (e.g. Figure 5; pp. 1647-1648, bridging para), which reads on step (i) of **clm 67**, the "partially digestion" of **clm 72**, the one strand digestion of **clm 73**, the limitations of **clm 75-77**.

The reference also teaches labeling the single stranded molecules using radio-nucleotides (e.g. p. 1648, col.1, para 1), which reads on step (ii) of **clm 67**.

The reference teaches generating "blunt ends" for the cDNA (e.g. p. 1647, col. 1, top of last para), and restriction digested to create a "sticky end" (e.g. Figure 5), which read on the restriction digestion of **clm 74** because the exonuclease digests the double stranded DNA from both ends (with ends derived from a blunt end).

The instant specification defines the term "global amplified cDNA" as "cDNA in which DNA molecules representing gene expression retain the same relative abundance as the mRNA transcripts from which they are derived" (spec. p. 6, para 2), which definition broadly encompass almost any cDNA derived from any mRNA transcripts. Thus, the cDNA taught by the reference reads on the global amplified cDNA of **clm 78**.

The reference also teaches the steps of amplifying cDNA from mRNA isolated from sample using homopolymer (oligo-dT) (e.g. p.1647, col.1, para 3-5), which reads on the cDNA preparation steps of **clm 79**.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Liao and Others

18. Claims 67, 68 and 72-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liao et al (Biochemistry. Vol. 20: 1646-1652; 1981), if necessary, in view of Struhl (Current Protocols in Molecular Biology. Section III: 3.4.1-3.4.11; 1993), Gelfand et al (US 5,561,058; 10/1/1996), Brady (Methods in Molecular and Cellular Biology. Vol.2: 17-25; 1990; cited in IDS), and Legerski (US 6,406,891; 6/18/02; filed 9/28/98).

Liao et al, throughout the publication, teach a method of producing single stranded and labeled DNA from double stranded DNA molecules using exonuclease digestion, as discussed above.

Liao et al do not expressly teach using "terminal transferase" to label the single stranded molecules, as recited in **clm 68**. However, Liao et al, teach using "terminal transferase" to label single stranded DNA molecules with radio-labeled nucleotides or non radio-labeled nucleotides

(e.g. p. 1647, col. 1, last para, col. 2, para 3). The Liao reference also does not expressly teach the various buffer conditions recited in **clms 80-97**.

Struhl, throughout the publication, teaches using terminal transferase to label single stranded nucleic acids (p. 3.4.1, para 1). The reference also teaches the advantages of using "terminal transferase" for labeling, which advantages include no template requirement (p. 3.6.1, para 2), and ability to label single stranded nucleic acid at the 3'-hydroxyl termini (p. 3.6.1, para 1).

Gelfand et al, throughout the patent, teach various conditions (with various buffers) for generating cDNA from mRNA (Abstract). The reference teaches using acetate buffers including potassium acetate (e.g. Claim 8), which reads on the acetate buffer of **clm 80**. The reference also teaches using polyT oligomer (or primer) that anneals to the polyA tail to amplify the isolated mRNA (e.g. col.9, lines 40+), which reads on the "T tract" of **clms 82 and 83**. The reference also teaches using dT primers with lengths such as 10-35 nucleotides (e.g. col. 9, lines 47+), which reads on the dT24 of **clm 92**.

The reference also teaches production of double stranded DNA having polyA and T tracts using polyT oligoes (e.g. claim 1; cols.9-10) and attaching specific primers using terminal transferase (e.g. col.21, 10+), which reads on the homopolymer tailing of **clm 87**, and terminal transferase of **clm 88**, as well as the amplification steps of **clms 95**.

The reference also teaches using Co^{+2} (such as $CoCl^2$) as the divalent ion for the Taq (DNA polymerase) and Tth (reverse transcriptase) mediated reactions (e.g. col.21, lines 34+). The reference also teaches the various divalent ions such as Mn^{+2}, Mg^{+2}, Co^{+2}, etc can be used interchangeably, and can be used in the form of Cl2 salts with concentrations ranging from 0.5-

10mM (e.g. col.21, lines28+, lines 34+, lines 48+), which reads on the amount of CoCl2 in **clms 92, 93, 94, 92, 96 and 97**.

The reference also teaches buffers comprising Tris (5-250 mM) buffer with pH 8.3 (e.g. col.22, lines 12+), KCl (1-200mM) monovalent salt (e.g. col.21, lines 55+), MgCl2 (0.5-10mM) divalent salt (col. 21, lines 52+), Mg(OAc)2 (1-20 nM) (e.g. col. 21, lines 48+), KOAc (1-20 mM) (e.g. col.21, lines 53), which read on the various buffers and salts (except the Tris Acetate) of **clms 84**, **89**, and **96**.

The reference teaches using NP-40 detergent with concentration of 0.01-0.05% for PCR reaction (e.g. col.22, lines 19+), Rnase inhibitor (e.g. col. 2, lines 15+), dNTP (at 200uM) (e.g. col. 28, lines 45+; col. 31, lines 15+), primes with concentration such as ~0.15uM (e.g. col.38, lines 58+), DNA polymerase (e.g. col. 32, lines 1+), which read on the components of NP40, dNTPs, and oligonucleotide of **clms 85, 86, 92, and 97**.

Brady et al, throughout the publication, teaches methods of preparing cDNA from mRNA with various reaction buffers (Abstract). The reference teaches using dT24 primers (e.g. p.18, para 1 under Methodology), BSA (e.g. p. 18, para 3 under Methodology), Rnase Inhibitor (e.g. p.18, para 1 under Methodology), glycogen (e.g. p.18, para 1 under Methodology and p.19, para 2), terminal transferase or TdT enzyme (e.g. p.18, para 2 under Methodology), and Triton X-100 (e.g. pp.18-19, bridging para), which read on the buffer components of glycogen, Rnase inhibitor, BSA, and Tdt of **clms 85, 90, 92 and 97**. The Brady reference also teaches the cDNA amplification steps (e.g. p.18, para 1 and 3 under Methodology) without using DTT, which reads on the method step of **clm 91**.

Legerski, throughout the patent, teach a method of RT-PCR to produce cDNA from mRNA (Abstract). The reference teaches using Tris-acetate buffer for an optimized condition for a thermo reverse transcriptase (e.g. col.10, lines 65+), which reads on the Tris-acetate buffer of **clms 81, 84, 89, and 96**.

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to label the single stranded DNA derived from an exonuclease digestion using terminal transferase, and to conduct the various reactions of preparing cDNA using the appropriate buffers and reagents for optimization of the said reactions.

A person of ordinary skill in the art would have been motivated at the time of the invention to use terminal transferase to label single stranded nucleic acids, because using terminal transferase for labeling is known in the art, and the enzyme offers the advantage of labeling single stranded DNA as well as no template requirement, as taught by Liao et al and Struhl.

A person of ordinary skill in the art would have been motivated at the time of the invention to use various buffer conditions such as acetate buffers for optimization of the various reactions such as reverse transcription and PCR amplification of the cDNA, because certain buffer conditions can produce optimal results such as taught by Legerski (e.g. optimal thermo reverse transcription with a thermo reverse transcriptase was obtained with "acetate" buffer; col.10, lines 65).

A person of ordinary skill in the art would have been motivated at the time of the invention to use (or not use) various components such as BSA, glycogen (a carrier), DTT, and

various monovalent and divalent ions in a reverse transcription reaction, terminal transferase reaction, and/or PCR reaction, because addition of these components to the said RT, Tdt and/or PCR reactions are known and routine in the art and offers to provide optimal reaction conditions, as taught by Liao et al, Struhl, Brady, Gelfand, and Legerski.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since all the above cited reference have demonstrated the success of conducting the RT, terminal transferase, and PCR amplification reactions under various buffer conditions with the common and conventional reagents. As taught by the said references, optimization of the said reactions by varying various reaction components are routine in the art, and thus a reasonable expectation of success can be expected without evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SL/
Art Unit 1639
7/5/07

/Jon D. Epperson/
Primary Examiner, AU 1639